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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/846,658	05/01/97	ADAIR J	CARP-0057

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EXAMINER	
REEVES, J	
ART UNIT	**PAPER NUMBER**
1642	13

DATE MAILED: 11/16/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/846,658	Applicant(s) Adair et al
	Examiner Julie E. Reeves, Ph.D.	Group Art Unit 1642

☒ Responsive to communication(s) filed on *May 1, 1997*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *24-31* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *24-31* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☒ received in Application No. (Series Code/Serial Number) *07/743,329*.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-23 have been canceled. Claims 24-31 have been added. The application is now complete with regards to preliminary Amendment E filed 8/5/98 which brought the case into compliance with the sequence requirements.

2. Applicants states that they wish to invoke an interference against an issued patent. Those remarks concerning the interference are held in abeyance until any allowable subject matter has been identified.

Specification

3. The disclosure is objected to because of the following informalities: the status of parent applications listed on the first line of the specification needs to be updated.

Appropriate correction is required.

Information Disclosure Statement

4. Page 10 of paper no 3 filed 5/1/97 states that copy of the Information Disclosure Statement field in parent applications Ser no 08/303,569 and 07/743,929 have been submitted. It is noted that these Information Disclosure Statement have not been filed with the case because they do not recite the correct serial number, 08/846,658. The Information Disclosure Statements will be considered once they are properly filed with the case and once the references have been submitted to the examiner.

Claim Rejections - 35 U.S.C. § 112

5. Claim 24-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

a. Claims 24 and 28 contain the limitation of "wherein each of said donor amino acids is adjacent to a CDR in the donor immunoglobulin sequence". The Preliminary Amendment filed 5/1/97 states that page 6 lines 25-35 and Figures 3-4 of the specification supports this limitation. This is not persuasive. In Figure 3-4, the broader term "near" is not commensurate in scope with the more narrowly claimed term "adjacent". On page 6, a series of potential substitutions are recited, of which only one, residue 49, is adjacent to any CDR. The specification does not provide support forth concept that only adjacent substitutions are envisaged, as encompassed by the newly added claim language "wherein each of said donor amino acids is adjacent to a CDR in the donor immunoglobulin sequence". Further, the specification clearly teaches that a wide range of substitutions are contemplated, some of which are "adjacent" and some or which are only "near" the CDRs. Applicant is required to either point to where the specification provides support for the narrower phrase or to remove it from the claims.

b. Concerning claims 27, 30 and 31, the specification uses the term OKT3 and OKT4, while the claims refer to the terms CD3 and CD4. It is the Examiner's belief that the CD nomenclature placed the earlier OKT names. However, in order to provide a clear file history, it

is suggested that applicant provide some evidence that claimed CD3 is the same as OKT3 found in the specification and that claimed CD4 is the same as OKT4 recited in the specification.

6. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

a. Claim 29 contains the limitation of "which specifically binds to an antigen with a binding affinity equivalent to that of a chimeric antibody formed from said donor immunoglobulin". In contrast, the response states that Claim 29 contains the limitation of "which specifically binds to an antigen with a binding affinity as binding as a chimeric antibody formed from said donor immunoglobulin" (copied from page 16 of the response). The Preliminary Amendment filed 5/1/97 states that page 23 lines 1-10 and Figure 29B of the specification supports this limitation. This is not persuasive. This application has no only 15 drawings and no Figure 29B is present in the instant application. Furthermore, the text on page 23, lines 1-10 recites specific amino acid substitutions and does not mention affinities. Applicant is required to either point to where the specification provides support for the phrase or to remove it from the claims.

Claim Rejections - 35 U.S.C. § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. Claims 24-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Queen et al, (US patent No 5,585,089 which was filed Jun 7 1995 and has 102(e) priority back to at least 12/28/90).

a. The newly added claims recite a humanized antibody having CDRs from a donor immunoglobulin and light and heavy chain variable regions form human acceptor immunoglobulin heavy and light chains, which specifically binds to an antigen with an affinity constant of at least 10^8 M^{-1} , wherein the humanized immunoglobulin comprises amino acid from a donor Ig framework outside of both the Kabat CDRs and the structural loop CDRs of the variable region, wherein the donor amino acids replace corresponding amino acids in the acceptor Ig heavy or light chain frameworks, and each of said donor amino acids is adjacent to a CDR in the donor Ig sequence. Other embodiments include humanized Igs with a 10^8 - 10^{12} M^{-1} affinity fir antigen; humanized Igs which bind to the IL-2 receptor; humanized Igs wherein the donor Ig is an anti-CD4 T-cell receptor antibody.

b. Also claimed is a humanized antibody having CDRs from a donor immunoglobulin and light and heavy chain variable regions form human acceptor immunoglobulin heavy and light chains, which specifically binds to an antigen with effective antigen binding affinity, wherein the humanized immunoglobulin comprises amino acid from a donor Ig framework outside of both the Kabat CDRs and the structural loop CDRs of the variable region, wherein the donor amino acids replace corresponding amino acids in the acceptor Ig heavy or light chain frameworks, and each of said donor amino acids is adjacent to a CDR in the donor Ig sequence. Other embodiments include wherein the humanized Ig binds antigen with an equivalent binding affinity as that of the chimeric antibody forme from said donor. Also claimed is humanized Ig which bind to human CD3 T-cell receptor and wherein the donor Ig is the anti-CD3 T-cell receptor antibody. It is noted that Applicants admit in the preliminary amendment filed 5/1/97, that claims 24-27 have been "substantially copied from claims 1, 5, 9 and 10 of Queen".

c. Queen et al teach methods of making humanized antibodies comprising CDRs and adjacent framework region amino acids from donor antibody. See, for example, Abstract, Figure 1B, 2A-B, 3B, 4B, 5B, 6A-B, 10A, 15, 26B, 30A-C, 36A-B, 40A-B, 44B. For explicit teaching of donor amino acid substitution of residues immediately adjacent, see category 3, col 3, lines 13-15, col 14, lines 30-43, col 38, lines 13-15, 39-40, col 45, lines 52-55, col 46, lines 3-5, col 65, line 47-48 and Claim 1, criteria I. Concerning the limitation of a humanized Ig comprising amino acid from a donor Ig framework outside of both the Kabat CDRs and the structural loop CDRs of

the variable region, Queen et al explicitly teaches the Kabat and Chothia CDRs, see page 9, lines 1-5 of 07/290,975 and page 13, lines 1-18 of 08/310,252. maintain

d. Concerning the 10^8 M^{-1} affinity limitation, Queen et al teaches this on col 3, lines 39-41, col 10, lines 60-63. Concerning the 10^8 M^{-1} - 10^{12} M^{-1} affinity limitation, Queen et al teaches this on col 10, lines 60-63, col 27, lines 53-56, col 30, lines 63-66 and claim 5. Queen et al teaches Ig which bind to the IL-2 receptor (col 16,, lines 32-37, col 17, line 4, col 20, line 40-col 23, line 12, col 25, line 7-col 26, line 41 and claim 9). Queen et al teaches using donor amino acid framework substitutions from outside either Kabat or Chothia (structural loop) CDRs (col 15, 22-67). Queen et al teach humanized Igs having affinity for a receptor found on T cells (CD25) (col 20-22 and 37-42) and all mAbs to Clusters of Differentiation (CD) markers which would include all T cell CDs (col 19, lines 35-41; col 23, lines 23-29; col 31, lines 34-40). Thus the limitations of the claims have been met.

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Reeves, Ph.D., whose telephone number is (703) 308-7553. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. Any inquiry of a general

nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Respectfully,

Julie E. Reeves, Ph.D.

Patent Examiner

(703) 308-7553

JULIE REEVES
PATENT EXAMINER